

Remarks

Reconsideration of this Application is respectfully requested.

Claims 10, 11, 25, 26, 40, 41 and 58-63 are pending in the application, with claims 10, 25, 40, 58, 60 and 62 being the independent claims.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Telephonic Interview

Applicants wish to thank the Examiner for the courtesy of a telephonic interview with Applicants' undersigned representative on September 12, 2005, during which the rejections under 35 U.S.C. §§ 112 and 103 were discussed.

II. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 10, 11, 25, 26, 40, 41 and 58-63 were rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. *See* Office Action, page 2. Applicants respectfully traverse this rejection.

The basis for this rejection is the Examiner's assertion that "the specification, while being enabling for treating amyloidosis in a subject with the combination of bathocuproine and clioquinol, does not reasonably provide enablement for other chelators specific for

copper combined with clioquinol." *See* Office Action, page 2. Applicants respectfully disagree and submit that the Examiner has not presented sufficient evidence or reasoning to support a *prima facie* case of non-enablement.

In order to establish a *prima facie* case of lack of enablement, the Examiner has the initial burden to set forth a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). To satisfy this burden, "it is incumbent upon the Patent Office. . . to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *See In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) (emphasis in original). Here, the Examiner has simply stated that:

Applicants have failed to provide guidance as to how the other chelators specific for copper combined with clioquinol is effective in treating amyloidosis. The level of experimentation needed to determine the other chelators specific for copper when combined with clioquinol would be able to treat amyloidosis is undue. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

See Office Action, page 4. The above assertion is not supported by any evidence, and the logic underlying the assertion is circular (according to the Examiner's reasoning, undue experimentation would be required to practice the invention because the level of

experimentation is supposedly undue). A *prima facie* case of non-enablement cannot be established on the basis of an unsupported, circular assertion.

In addition, the teachings in the specification strongly suggest that identifying chelators specific for copper that, when combined with clioquinol, treat amyloidosis in a subject, would not have required undue experimentation. For example, Example 7, at pages 84-85, shows the extent of A β solubilization in an *in vitro* assay in the presence of bathocuproine (BC), clioquinol (CQ), and a combination of BC and CQ. As demonstrated in this example, A β solubilization is significantly enhanced in the presence of BC+CQ. See Table 4 and Figure 26. As noted in Applicants' Reply Under 35 U.S.C. § 1.111, filed January 11, 2005, at page 7, *in vitro* results with chelators are indicative of the therapeutic results that are obtained when the chelators are administered *in vivo*. Thus, a person of ordinary skill in the art, in view of the experiment set forth in Example 7, could have easily screened a multitude of chelators specific for copper to identify those that, when combined with clioquinol, treat amyloidosis in a subject. There is no evidence of record to suggest that this is not the case.

Finally, the Examiner has acknowledged that the specification is enabling for the treatment of amyloidosis in a subject using a combination of bathocuproine and clioquinol. See Office Action, page 2. Applicants note that the critical characteristic of bathocuproine that renders it useful for the treatment of amyloidosis when combined with clioquinol is that it is *specific for copper*. The present claims specify this characteristic. Since the Examiner has acknowledged the enablement provided for the combination of bathocuproine and

clioquinol to treat amyloidosis, there is no logical reason to believe that the use of other chelators having the same critical characteristic as bathocuproine (*i.e.*, being specific for copper), when combined with clioquinol, would not likewise be enabled by the specification.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 10, 11, 25, 26, 40, 41 and 58-63 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,022,879 to Crow *et al.* ("Crow") in view of U.S. Patent No. 5,980,914 to Gerolymatos ("Gerolymatos"). *See* Office Action, pages 4-5. Applicants respectfully traverse this rejection.

According to the Examiner:

The instant rejection is based upon the well-established principle of patent law that no invention resides in combining 2 or more ingredients of known character, where the results obtained are no more than the additive effects of the individual ingredients.

See Office Action, page 5. The Examiner has not cited any legal authority to support this so-called "well-established principle of patent law," and Applicants are not aware of any such authority. Applicants are, however, aware of the rule that a *prima facie* case of obviousness cannot be established unless there is some suggestion or motivation to combine the cited

references. *See* M.P.E.P. § 2143; *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). As noted in M.P.E.P. § 2143.01:

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.

There is nothing in either Crow or Gerolymatos to suggest combining a chelator specific for copper with clioquinol in order to treat amyloidosis. Thus, a *prima facie* case of obviousness has not been established.

Crow refers to the use of bathocuproine for treating amyotrophic lateral sclerosis (ALS). *See* Crow, column 4, lines 30-35. Crow does not suggest combining bathocuproine with any other active ingredient, much less another chelator. Gerolymatos refers to the use of clioquinol for treating Parkinson's disease. *See* Gerolymatos, column 1, lines 5-8. Gerolymatos mentions the combination of clioquinol and vitamin B₁₂; however, the asserted purpose of combining vitamin B₁₂ with clioquinol in Gerolymatos is simply to counteract the vitamin B₁₂ deficiency that supposedly results from the administration of clioquinol. *See* Gerolymatos, column 5, lines 15-18. A person of ordinary skill in the art, in view of the cited references would find no reason to combine bathocuproine with clioquinol.

Importantly, the Examiner has not pointed to anything in either Crow or Gerolymatos that would have suggested combining a chelator specific for copper with clioquinol. Thus, a *prima facie* case of obviousness has not been established. The Examiner's statement regarding the supposed need for "more than additive effects" when ingredients of known character are combined is legally insufficient to support the obviousness rejection¹. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

¹ Notwithstanding the fact that there is no legal authority to support the requirement for "more than additive effects" when two or more ingredients of known character are combined in order for the combination to be patentable, Applicants note that the combination of bathocuproine and clioquinol resulted in a greater than additive effect in the in vitro A β solubilization assay shown in Example 7 of the present application. (See page 84, Table 4, and Figure 26.)

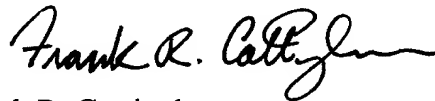
Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Frank R. Cottingham
Attorney for Applicants
Registration No. 50,437

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

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